claims 2-18 will be in the application. Based on what appears in the final Action, claims 2-18 should all be allowable, whereby the above amendment should place the present application in condition for allowance. Accordingly, applicants respectfully request favorable consideration, entry of the amendments presented above and allowance.

Claims 8-17 have been allowed, whereby applicants understand that these claims are deemed by the PTO to define novel and unobvious subject matter under §§102 and 103. Similarly, claims 6 and 7 have only been objected to, i.e. these claims have not been rejected on the basis of any prior art, and again applicants understand that these claims are deemed by the PTO to define novel and unobvious subject matter under §§102 and 103.

Claim 6 has been redrafted in independent form, and therefore should be in condition for formal allowance. Claim 7 depends from claim 6, and therefore should be in condition for formal allowance. Claims 2-5 have been amended to depend from claim 6, and these claims also should now be in condition for formal allowance. New claim 18 is the same as claim 4, except dependent from claim 3 instead of claim 6, and therefore new claim 18 should also be allowed as being ultimately dependent from allowable claim 6.

Claim 1 has been deleted, leaving **only** allowable claims. Accordingly, the amendments presented above should place the present application in condition for allowance.

As regards the rejection of claim 1-5 as anticipated under §102, applicants need no longer address this matter in view of the cancellation of claim 1 and the amendment of claims 2-5 to make them dependent on allowable claim 6.

One possible issue remains, not raised in the final Action. Thus, a review of the present application has revealed that five documents mentioned in the specification (bottom of page 1; page 3, lines 18-21; top of page 4; sentence spanning pages 4 and 5; and page 15, lines 5 and 6) were not cited in an Information Disclosure Statement (IDS), and copies were not provided. To complete the record, applicants file herewith copies of these five documents along with a form PTO/SB/57 upon which these documents are listed. Also listed is a sixth document, copy also attached, which is a newly found scientific document.

Of these, document AH is from a Japanese Scientific journal and is in Japanese. Accordingly, a partial translation, i.e. a translation of pertinent portions of this document, is also enclosed herewith.

Except for the newly discovered document AI, the possible relevance of each of these documents appears in applicants' specification. In addition, each one of documents AD-AG and AI is in the English language, and thus can be easily perused; the attached partial translation of AH can also be easily perused. Applicants respectfully request the examiner to review these documents and initial the form PTO/SB/57 so that these documents will appear on the face of the resultant patent.

Favorable consideration and earlier formal allowance are respectfully urged.

Respectfully submitted,

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Version with Markings to Show Changes Made

6. (amended) ~~The~~ A method ~~according to claim 1~~ of diagnosing metasasis of malignant tumor to bone using both a marker that reflects the activity of osteoblasts and a marker that reflects the action of osteoclasts, ~~which is~~ based on the value of a crossover index or the ratio between a marker associated with the phase of osteoblast proliferation and matrix formation and the measured value of the marker that reflects the action of osteoclasts, or on the value of a crossover index or the ratio between a marker associated with the phase of calcification and a marker associated with the phase of matrix maturation and the measured value of a marker associated with bone type I collagen, whereby the amelioration of bone metastasis or therapeutic effect and the degree of the exacerbation of bone metastasis are diagnosed correctly by monitoring said two markers, one associated with osteoblasts and targeted to evaluation of therapeutic effect, and the other associated with osteoclasts and targeted to evaluation of worsening of the disease.

2. (amended) The method of claim ~~1~~6, wherein the marker that reflects the activity of osteoblasts is:

(1) a marker associated with the phase of osteoblast proliferation and matrix formation and a marker associated with the phase of calcification; or

(2) a marker associated with the phase of matrix maturation and a marker associated with the phase of calcification.

3. (twice Amended) The method according to claim ~~1~~6, wherein the marker that reflects the activity of osteoblasts is:

(1) Carboxyterminal propeptide of type I procollagen or Amino terminal propeptide of type I procollagen and osteocalcin; or

(2) Bone specific alkaliphosphatase and osteocalcin.

4. (amended) The method according to claim ~~1~~6, wherein the marker that reflects the action of osteoclasts is a marker associated with bone type I collagen.

5. (Amended) The method according to claim ~~1~~6, wherein the marker that reflects the action of osteoclasts is deoxypyridinoline and/or Carboxyterminal telopeptide of type I collagen.